REMARKS

New claims 26-79 are pending in the application for the Examiner's review and consideration. Applicant appreciates the Examiner's recognition of patentable subject matter in claims 8, 10, 11, and 20-22. Claims 1-25 were canceled and replaced with new claims 26-79. New claims 26-79 more clearly describe the invention and add no new matter. New claims 26-77 simply rewrite claim 1 as four separate independent claims and make minor changes in the amounts. Claim 1 recited four possible embodiments of the invention, *i.e.*, (a) active compound and a polar solvent; (ai) active compound, polar solvent, and propellant; (b) active compound and non-polar solvent; and (bi) active compound, non-polar solvent, and propellant. Each of these embodiments is now recited individually in independent claims 26, 39, 54, and 62. Claims 26 and 53 were amended to recite that the spray composition is propellant free (*See, e.g.*, Specification, Examples 1a, e, f, g, and h; 2a, c, e and g; 3a, and b; 4d; 5a and c; 6a-c; 7a; 8a; 9b; 10; 11a, b, and e). The dependent claims correspond to the originally filed dependent claims. New claim 78 rewrites claim 24 but recites the active compounds disclosed in the specification at page 6, lines 24-25. New claim 79 rewrites original claim 25. As no new matter has been added, Applicant respectfully submits that these amendments be entered. Applicant respectfully submits that all claims are in condition for allowance.

THE INVENTION

The invention relates to buccal spray compositions for transmucosal administration of a pharmacologically active compound and a polar solvent (claims 26-36); a pharmacologically active compound, a polar solvent, and a propellant (claims 39-50); a pharmacologically active compound and a non-polar solvent (claims 53-59 and 78-79) or a pharmacologically active compound, a non-polar solvent, and a propellant (claims 62-77). The invention further relates to a method of administering a pharmacologically active compound to a mammal by spraying the oral mucosa of the mammal with a composition of the invention (claims 37-38, 51-52, 60-61, and 76-77).

THE REJECTION UNDER 35 U.S.C. § 103(a)

Claims 1-2, 18-19, and 23-24 were rejected under 35 U.S.C. § 103(a) as being obvious over U.S. Patent No. 5,474,759 to Fassberg et al. ("Fassberg") for the reasons set

forth on pages 2-3 of the Office Action. The rejection of claims 1-2, 18-19, and 23-24 are rendered moot by the cancellation of these claims. Applicant, however, will address the rejection with respect to new claims 26-79.

Fassberg discloses an aerosol formulation that contains a medicament and 1,1,1,2,3,3,3-heptafluoropropane (*i.e.*, "propellant 227" or "Freon 227") as a propellant. Fassberg discloses that this formulation can be used for oral or nasal inhalation, but does not disclose buccal administration.

Fassberg, however, does not render the present invention obvious. First, Applicant notes that new independent claims 26 and 53 (that correspond to embodiment (a) and (b) of original claim 1) recite that the composition is propellant free. The buccal spray compositions disclosed in claims 26 and 53 do not require a propellant to be administered and can be administered, for example, from a container equipped with a pump spray (*See, e.g.*, Specification, page 2, line 31 to page 3, line 14). In contrast, the formulation disclosed in Fassberg requires a propellant, *i.e.*, Freon 227. There is absolutely no disclosure or suggestion in Fassberg of a propellant-free composition. Therefore, there is no basis to make the claimed propellant-free compositions in view of Fassberg's propellant compositions. Accordingly, Fassberg does not render independent claims 26 and 53 or claims that depend therefrom obvious.

With regard to new independent claims 39 and 62 (that correspond to embodiments (ai) and (bi) of original claim 1), the propellant recited in these claims is a C_3 to C_8 hydrocarbon of linear or branched configuration. In contrast, Fassberg discloses a fluorinated propellant, *i.e.*, 1,1,1,2,3,3,3-heptafluoropropane. In the first instance 1,1,1,2,3,3,3-heptafluoropropane (*i.e.*, "Freon 227") is not a non-halogenated C_3 to C_8 hydrocarbon. In addition, Fassberg does not disclose or suggest the use of non-halogenated hydrocarbons. Moreover, the Examiner has not provided any reasons why, in view of Fassberg, a person of ordinary skill in the art would substitute a non-halogenated C_3 to C_8 hydrocarbon propellant, used in the present invention, for the halogenated Freon 227 described in Fassberg. Furthermore, the specification of the present application clearly states that the propellants used in the claimed compositions are non-Freon propellants (*See, e.g.*, Specification, page 4, lines 26-27). Since all Freon propellants are fluorinated, there is no possibility that the claims could be read as including a fluorinated propellant such as

disclosed in Fassberg. There is absolutely no disclosure or suggest in Fassberg of a buccal spray composition that comprises, as the propellant, a C_3 to C_8 hydrocarbon, as presently claimed. Accordingly, Fassberg does not render independent claims 39 and 62 or claims that depend therefrom obvious. For the above reasons, Applicants respectfully request that the rejection under 35 U.S.C. § 103(a) be withdrawn.

THE DOUBLE PATENTING REJECTION

Claim 25 was provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 2 of U.S. patent no. 5,995,098 ("the '098 patent"). The rejection of claim 25 is rendered moot by the cancellation of that claim. Applicant, however, will address the rejection with respect to new claim 79 that is similar to original claim 25.

Claims 1-7, 9, and 12-13 were rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over the claims of U.S. patent no. 6,110,486 in view of Fassberg. The rejection of these claim is rendered moot by the cancellation of these claims. Applicant, however, will address the rejection with respect to the new claims.

Claims 1-2, 9, 12-19, and 23-24 were rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over the '098 patent in view of Fassberg. The rejection of these claim is rendered moot by the cancellation of these claims. Applicant, however, will address the rejection with respect to the new claims.

In response to the obviousness-type double-patenting rejection, Applicant will provide a Terminal Disclaimer disclaiming the terminal part of any patent granted on the above identified application which would extend beyond the expiration date of U.S. patent no. 5,995,098 or U.S. patent no. 6,110,486 when all art rejections have been overcome.

CONCLUSIONS

All claims are believed to be in condition for allowance. Should the Examiner have any questions, Applicant respectfully invites the Examiner to contact the undersigned attorneys for Applicant to arrange for an interview in an effort to expedite the prosecution of this matter.

A fee of $774.00 is believed to be due for the addition of 34 claims in excess of 20 (*i.e.*, 29 in excess of the 25 originally filed) and 3 independent claims in excess of 3. Please charge the required fee to Pennie & Edmonds LLP Deposit Account No. 16-1150.

Respectfully submitted,

Date August 23, 2002

Paul E. Dietze (Reg. No. 45,627)
for: Thomas G. Rowan (Reg. No. 34,419)

PENNIE & EDMONDS LLP
1667 K Street, N.W.
Washington, DC 20006
(202) 496-4400

Enclosure

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Appendix A

Currently Pending Claims

Application No.: 09/537,118; Filed: March 29, 2000

26. (New) A propellant free buccal spray composition for transmucosal administration of a pharmacologically active compound comprising:

an active compound in an amount of between 0.001 and 60 percent by weight of the total composition selected from the group consisting of biologically active peptides, central nervous system acting amines, sulfonyl ureas, antibiotics, antifungals, sleep inducers, antiasthmatics, antiemetics, antivirals, histamine H-2 receptor antagonists, barbiturates, prostoglandins, and bronchial dilators selected from terbutaline and theophyline; and

an polar solvent in an amount between 30 and 99 percent by weight of the total composition.

27. (New) The composition of claim 26, further comprising a flavoring agent in an amount of between 0.1 and 10 percent by weight of the total composition.

28. (New) The composition of claim 27, wherein the polar solvent is present in an amount between 37 and 98 percent by weight of the total composition, the active compound is present in an amount between 0.005 and 55 percent by weight of the total composition, and the flavoring agent is present in an amount between 0.5 and 8 percent by weight of the total composition.

29. (New) The composition of claim 28, wherein the polar solvent is present in an amount between 59 and 97 percent by weight of the total composition, the active compound is present in an amount between 0.01 and 40 percent by weight of the total composition, and the flavoring agent is present in an amount between 0.75 and 7.5 percent by weight of the total composition.

30. (New) The composition of claim 26, wherein the polar solvent is selected from the group consisting of polyethylene glycols having a molecular weight between 400 and

1000, C_2 to C_8 mono- and poly-alcohols, and C_7 to C_{18} alcohols of linear or branched configuration.

31. (New) The composition of claim 26, wherein the polar solvent comprises aqueous polyethylene glycol.

32. (New) The composition of claim 26, wherein the polar solvent comprises aqueous ethanol.

33. (New) The composition of claim 26, wherein the active compound is selected from the group consisting of cyclosporin, clozapine, zidevudine, erythromycin, ondansetron, cimetidine, phenytoin, carboprost thromethamine, valerin, and pharmaceutically acceptable salts thereof.

34. (New) The composition of claim 27, wherein the flavoring agent is selected from the group consisting of synthetic or natural oil of peppermint, oil of spearmint, citrus oil, fruit flavors, sweeteners, and mixtures thereof.

35. (New) The composition of claim 27, wherein the polar solvent is present in an amount between 75 and 85 percent by weight of the total composition, the active compound is cyclosporin present in an amount between 15 and 25 percent by weight of the total composition, and the flavoring agent is present in an amount between 0.1 and 5 percent by weight of the total composition.

36. (New) The composition of claim 27, wherein the polar solvent is present in an amount between 19 and 90 percent by weight of the total composition, the active compound is ondansetron hydrochloride present in an amount between 2.5 and 15 percent by weight of the total composition, and the flavoring agent is present in an amount between 1 and 10 percent by weight of the total composition.

37. (New) A method of administering a pharmacologically active compound to a mammal comprising spraying the oral mucosa of said mammal with the composition of claim 26.

38. (New) The method of claim 37, wherein the amount of the spray is predetermined.

39. (New) A buccal spray composition for transmucosal administration of a pharmacologically active compound comprising:

an active compound in an amount of between 0.1 and 25 percent by weight of the total composition selected from the group consisting of biologically active peptides, central nervous system acting amines, sulfonyl ureas, antibiotics, antifungals, sleep inducers, antiasthmatics, antiemetics, antivirals, histamine H-2 receptor antagonists, barbiturates, prostoglandins, and bronchial dilators selected from terbutaline and theophyline;

a polar solvent in an amount between 10 and 97 percent by weight of the total composition; and

a propellant in an amount between 2 and 10 percent by weight of the total composition, wherein said propellant is a C_3 to C_8 hydrocarbon of linear or branched configuration.

40. (New) The composition of claim 39, further comprising a flavoring agent in an amount between 0.05 and 10 percent by weight of the total composition.

41. (New) The composition of claim 40, wherein the polar solvent is present in an amount between 20 and 97 percent by weight of the total composition, the active compound is present in an amount between 0.1 and 15 percent by weight of the total composition, the propellant is present in an amount between 2 and 10 percent by weight of the composition, and the flavoring agent is present in an amount between 0.1 and 5 percent by weight of the total composition.

42. (New) The composition of claim 41, wherein the polar solvent is present in an amount between 25 and 97 percent by weight of the total composition, the active compound

is present in an amount between 0.2 and 25 percent by weight of the total composition, the propellant is present in an amount between 2 and 10 percent by weight of the composition, and the flavoring agent is present in an amount between 0.1 and 2.5 percent by weight of the total composition.

43. (New) The composition of claim 39, wherein the polar solvent is selected from the group consisting of polyethyleneglycols having a molecular weight between 400 and 1000 g/mol, C_2 to C_8 mono- and poly-alcohols, and C_7 to C_{18} alcohols of linear or branched configuration.

44. (New) The composition of claim 39, wherein the polar solvent comprises aqueous polyethylene glycol.

45. (New) The composition of claim 39, wherein the polar solvent comprises aqueous ethanol.

46. (New) The composition of claim 39, wherein the active compound is selected from the group consisting of cyclosporin, clozapine, zidevudine, erythromycin, ondansetron, cimetidine, phenytoin, carboprost thromethamine, valerin, and pharmaceutically acceptable salts thereof.

47. (New) The composition of claim 40, wherein the flavoring agent is selected from the group consisting of synthetic or natural oil of peppermint, oil of spearmint, citrus oil, fruit flavors, sweeteners, and mixtures thereof.

48. (New) The composition of claim 40, wherein the polar solvent is present in an amount between 55 and 72 percent by weight of the total composition, the active compound is cyclosporin present in an amount between 15 and 25 percent by weight of the total composition, the propellant is present in an amount between 2 and 10 percent by weight of the composition, and the flavoring agent is present in an amount between 0.1 and 5 percent by weight of the total composition.

49. (New) The composition of claim 40, wherein the polar solvent is present in an amount between 19 and 90 percent by weight of the total composition, the active compound is ondansetron hydrochloride present in an amount between 2.5 and 15 percent by weight of the total composition, the propellant is present in an amount between 2 and 10 percent by weight of the composition, and the flavoring agent is present in an amount between 1 and 10 percent by weight of the total composition.

50. (New) The compsition of claim 39, wherein the propellant is selected from the group consisting of propane, *N*-butane, *iso*-butane, *N*-pentane, *iso*-pentane, *neo*-pentane, and mixtures thereof.

51. (New) A method of administering a pharmacologically active compound to a mammal comprising spraying the oral mucosa of said mammal with the composition of claim 39.

52. (New) The method of claim 51, wherein the amount of the spray is predetermined.

53. (New) A propellant free buccal spray composition for transmucosal administration of a pharmacologically active compound comprising:

an active compound in an amount between 0.005 and 55 percent by weight of the total composition selected from the group consisting of biologically active peptides, central nervous system acting amines, sulfonyl ureas, antibiotics, antifungals, sleep inducers, antiasthmatics, antiemetics, antivirals, histamine H-2 receptor antagonists, barbiturates, prostoglandins, and bronchial dilators selected from terbutaline and theophyline; and

a non-polar solvent in an amount between 30 and 99 percent by weight of the total composition.

54. (New) The composition of claim 53, further comprising a flavoring agent in an amount between 0.1 and 10 percent by weight of the total composition.

55. (New) The composition of claim 54, wherein the non-polar solvent is present in an amount between 69 and 99 percent by weight of the total composition, the active compound is clozepine in an amount from between 0.5 and 30 percent by weight of the total composition, and the flavoring agent is present in an amount between 0.1 and 5 percent by weight of the total composition.

56. (New) The composition of claim 53, wherein the active compound is selected from the group consisting of cyclosporin, clozapine, zidevudine, erythromycin, ondansetron, cimetidine, phenytoin, carboprost thromethamine, valerin, and pharmaceutically acceptable salts thereof.

57. (New) The composition of claim 54, wherein the flavoring agent is selected from the group consisting of synthetic or natural oil of peppermint, oil of spearmint, citrus oil, fruit flavors, sweeteners, and mixtures thereof.

58. (New) The composition of claim 53, wherein the solvent is selected from the group consisting of (C_2-C_{24}) fatty acid (C_2-C_6) esters, C_7-C_{18} hydrocarbons of linear or branched configuration, C_2-C_6 alkanoyl esters, and triglycerides of C_2-C_6 carboxylic acids.

59. (New) The composition of claim 53, wherein the solvent is miglyol.

60. (New) A method of administering a pharmacologically active compound to a mammal comprising spraying the oral mucosa of said mammal with the composition of claim 53.

61. (New) The method of claim 60, wherein the amount of the spray is predetermined.

62. (New) A buccal spray composition for transmucosal administration of a pharmacologically active compound comprising:

an active compound in an amount between 0.05 and 50 percent by weight of the total composition selected from the group consisting of biologically active peptides,

central nervous system acting amines, sulfonyl ureas, antibiotics, antifungals, sleep inducers, antiasthmatics, antiemetics, antivirals, histamine H-2 receptor antagonists, barbiturates, prostoglandins, and bronchial dilators selected from terbutaline and theophyline; and

a non-polar solvent in an amount between 20 and 85 percent by weight of the total composition; and

a propellant in an amount between 5 and 70 percent by weight of the total composition, wherein said propellant is a C_3 to C_8 hydrocarbon of linear or branched configuration.

63. (New) The composition of claim 62, further comprising a flavoring agent in an amount of between 0.1 and 10 percent by weight of the total composition.

64. (New) The composition of claim 62, wherein the active compound is selected from the group consisting of cyclosporin, clozapine, zidevudine, erythromycin, ondansetron, cimetidine, phenytoin, carboprost thromethamine, valerin, and pharmaceutically acceptable salts thereof.

65. (New) The composition of claim 63, wherein the flavoring agent is selected from the group consisting of synthetic or natural oil of peppermint, oil of spearmint, citrus oil, fruit flavors, sweeteners, and mixtures thereof.

66. (New) The composition of claim 62, wherein the propellant is present in an amount between 5 and 70 percent by weight of the total composition, the non-polar solvent is present in an amount between 25 and 85 percent by weight of the total composition, the active compound is present in an amount from between 0.1 and 40 percent by weight of the total composition, and the flavoring agent is present in an amount between 1 and 8 percent by weight of the total composition.

67. (New) The composition of claim 66, wherein the propellant is present in an amount between 20 and 70 percent by weight of the total composition, the non-polar solvent is present in an amount between 30 and 75 percent by weight of the total composition, the active compound is present in an amount from between 0.25 and 35 percent by weight of the

total composition, and the flavoring agent is present in an amount between 2 and 7.5 percent by weight of the total composition.

68. (New) The composition of claim 62, wherein the propellant is selected from the group consisting of propane, *n*-butane, *iso*-butane, *n*-pantane, *iso*-pentane, *neo*-pentane, and mixtures thereof.

69. (New) The composition of claim 68, wherein the propellant is *n*-butane or *iso*-butane and has a water content of not more than 0.2 percent and a concentration of oxidizing agents, reducing agents, Lewis acids, and Lewis bases of less than 0.1 percent.

70. (New) The composition of claim 62, wherein the solvent is selected from the group consisting of (C_2-C_{24}) fatty acid (C_2-C_6) esters, C_7-C_{18} hydrocarbons of linear or branched configuration, C_2-C_6 alkanoyl esters, and triglycerides of C_2-C_6 carboxylic acids.

71. (New) The composition of claim 62, wherein the solvent is miglyol.

72. (New) The composition of claim 62, wherein the propellant is present in an amount between 15 and 70 percent by weight of the total composition, the non-polar solvent is present in an amount between 20 and 85 percent by weight of the total composition, the active compound is clozepine in an amount between 0.5 and 30 percent by weight of the total composition, and the flavoring agent is present in an amount between 1 and 5 percent by weight of the total composition.

73. (New) The composition of claim 62, wherein the propellant is present in an amount between 15 and 70 percent by weight of the total composition, the non-polar solvent is present in an amount between 20 and 85 percent by weight of the total composition, the active compound is zidovudine in an amount between 25 and 35 percent by weight of the total composition, and the flavoring agent is present in an amount between 1 and 5 percent by weight of the total composition.

74. (New) The composition of claim 62, wherein the propellant is present in an amount between 5 and 60 percent by weight of the total composition, the non-polar solvent is present in an amount between 20 and 85 percent by weight of the total composition, the active compound is carboprost in an amount between 0.5 and 5 percent by weight of the total composition, and the flavoring agent is present in an amount between 0.1 and 10 percent by weight of the total composition.

75. (New) The composition of claim 62, wherein the propellant is present in an amount between 5 and 60 percent by weight of the total composition, the non-polar solvent is present in an amount between 50 and 85 percent by weight of the total composition, the active compound is terbutaline in an amount between 0.5 and 6 percent by weight of the total composition, and the flavoring agent is present in an amount between 0.01 and 10 percent by weight of the total composition.

76. (New) A method of administering a pharmacologically active compound to a mammal comprising spraying the oral mucosa of the mammal with the composition of claim 62.

77. (New) The method of claim 76, wherein the amount of the spray is predetermined.

78. (New) A buccal spray composition for transmucosal administration of a pharmacologically active compound comprising:

an active compound in an amount between 0.1 and 25 percent by weight of the total composition selected from the group consisting of antihistamines, alkaloids, hormones, benzodiazepines and analgesics;

a polar solvent in an amount between 10 and 97 percent by weight of the total composition; and

propellant in an amount between 2 and 10 percent by weight of the total composition, wherein said propellant is a C_3 to C_8 hydrocarbon of linear or branched configuration.

79. (New) A buccal spray composition for transmucosal administration of a pharmacologically active compound comprising:

an active compound in an amount between 0.005 and 55 percent by weight of the total composition selected from the group consisting of antihistamines, alkaloids, hormones, benzodiazepines, and narcotic analgesics;

a non-polar solvent in an amount between 30 and 99 percent by weight of the total composition.